for further and perhaps, in the end, more costly sickness. Be this as it may, prevention of illness, injury and emotional disturbance is clearly desirable. When it is successful, morbidity is avoided, mortality may be delayed and the quality of life of persons and communities is enhanced.

But, as Holmes points out, prevention is not always easy to sell as a segment of medicine which should receive a fair share of professional interest and public support. Perhaps those interested in advancing preventive medicine should begin to define its dimensions more clearly because at the moment, as is true for medicine itself, these dimensions seem too general and almost all-inclusive. However, those who espouse preventive medicine and seek support for it also have a special problem. By definition whatever is prevented never happens, and therefore cannot be measured in dollars or anything else. It would seem that more attention might be given to this and ways should be sought to measure the cost-effectiveness of prevention. For instance, poliomyelitis has been prevented. Would it now be possible to extrapolate the preimmunization incidence of poliomyelitis into what would have been the annual cost of the care of the projected victims in 1980 dollars? These would have been the health care costs in 1980 for this condition had not the disease been prevented. Such an approach to estimating the "prevented" costs might help to generate the interest in and support for preventive medicine which Holmes seeks.

But this writer cannot help wondering, when all is said and done, whether we really want to prevent everything. Some things, yes; but do we really mean all risk of illness, injury or emotional stress? Where will be the romance in living if there are no risks? This is especially true where human nature and human behavior are involved. People like to take risks. In a sense, the opportunity to take a chance is what life is all about, especially in a free society.

—MSMW

Complications of Anticoagulant Therapy

THE CASE REPORT on anticoagulant-induced bleeding of ovarian origin in this issue prompted this editorial. Students of anticoagulant therapy recognize the ovary as a well-known source of intraperitoneal bleeding.[1] In fact, 300 cases of intraperitoneal bleeding of ovarian origin were reported by 1937—before the era of anticoagulant therapy.[2] However, one reason for the low incidence of anticoagulant-induced ovarian hemorrhaging is that it occurs mainly in ovulating, menstruating women from a corpus luteum in the vascular premenstrual phase. Furthermore, anticoagulant therapy usually is prescribed for disorders that occur in nonovulating women, such as thrombophlebitis during pregnancy or puerperium and coronary artery disease following menopause.

There are many well-described bleeding syndromes associated with anticoagulant therapy that often simulate those of patients with congenital hemophilia. The occurrence of compression neuropathy is well known, particularly after percutaneous needle puncture of the brachial or femoral artery. Such complications underscore the need for obtaining arterial blood specimens from the radial artery, where manual pressure can be applied firmly after the puncture, in patients taking anticoagulant drugs.[3] Spontaneous retroperitoneal hemorrhage often appears as an acute femoral neuropathy because the extravasated blood passes underneath the tight fascia of the iliac fossa.[4] Anticoagulant-induced hemopericardium with tamponade can occur even in the absence of myocardial infarction or pericarditis, or after a cardiac surgical operation.[5] Intrarenal hematoma, adrenal hemorrhage, and even a hematoma within the abdominal rectus sheath[6] can occur during anticoagulant therapy. Often, the first symptom is acute abdominal pain, as it was in the case reported by Dr. Honoré.

The most serious bleeding syndromes during anticoagulant therapy are those of the central nervous system and the gastrointestinal tract. Gastrointestinal bleeding is often associated with intramural hematomas of the small intestine that have distinctive radiographic patterns.[7] These hematomas usually resolve with conservative management, and surgical extirpation of the hemorrhagic segment is contraindicated. Intracranial hemorrhage has been reported in more than 100 patients, most of whom died.[8] Spinal epidural hematomas also occur, which can be painless. A lumbar puncture may produce paraplegia, even when carried out shortly before the administration of anticoagulant drugs.[9]

The use of an orally given anticoagulant drug during pregnancy is dangerous because, unlike the

large and highly charged molecule of heparin, the small uncharged molecules of the drug equilibrate across the placenta into the fetal circulation. Thus, anticoagulant medication given orally to the mother in the first trimester can act as an abortifacient and cause fetal wastage, or as a teratogen, causing congenital anomalies such as skeletal enchondromatosis in the newborn.[10] These drugs administered in the third trimester can cause stillbirths as well as central nervous system damage secondary to the fetal intracranial bleeding that is frequently associated with the forces of labor. Whenever possible, heparin should be the only anticoagulant drug given to pregnant patients. Finally, anticoagulant-induced necrosis of the skin and of subcutaneous tissues, unrelated to the hypoprothrombinemic effect, has been reported in more than 150 patients, especially in obese women. It affects the fatty tissue of the breasts, buttocks, thighs and abdomen. The necrosis is caused by hemorrhagic infarctions associated with necrotizing arteritis and venous thrombosis, which are induced somehow by the orally given anticoagulant drug. These complications generally occur during the first two weeks of therapy.[11]

How can these hemorrhagic complications of anticoagulant therapy be avoided? Because bleeding usually results from an extension of the pharmacologic effect of these drugs, both physicians and, especially, patients must avoid all possible factors that can augment their hypoprothrombinemic effect. The three cornerstones of safe anticoagulant therapy are a carefully selected, well-informed, cooperative *patient* who is closely supervised by an experienced *physician* who is aided by suitable *laboratory* facilities for the accurate control of therapy.

Long-term anticoagulant therapy of a patient who is not in the hospital is hazardous unless the patient (or someone residing with him or her) is capable of taking responsibility for the therapy, has sufficient literacy in the mutual language of physician and patient and the visual acuity to read instructions, is intelligent enough to understand the serious nature of the therapy and the need for close control and supervision, and has shown consistency in keeping appointments.[12] Initially, the patient must be thoroughly examined by the physician to detect bleeding or any potentially hemorrhagic lesions and to identify absolute and relative medical contraindications to anticoagulant therapy. The physician must assess the risk of intracranial hemorrhaging in hypertensive patients and must screen all patients for potential sources of gastrointestinal bleeding.[13] Although the complicated details of laboratory control of anticoagulant therapy are beyond the scope of this editorial, the thorough report that was just published by an international panel of experts[14] should be consulted by all physicians who prescribe orally administered anticoagulant drugs.

Administration of anticoagulants on a long-term basis is a highly specialized form of treatment, and clinics devoted solely to these patients have been established. The highest therapeutic efficacy and lowest hemorrhagic toxicity of these drugs have been achieved in small European countries, such as Norway and Holland, where specialized centers have been established by physicians expert both in the clinical management and the laboratory control of this therapy. Risk factors for hemorrhagic complications during long-term therapy include poor supervision of the patient, use of orally administered anticoagulant drugs despite medical contraindications, poor laboratory control of the drug dosage, administration of large initial doses or a dosage that is too intense for the patient, concomitant administration of drugs, such as acetylsalicylic acid or barbiturates that interact with anticoagulant drugs given orally, and anticoagulant treatment of elderly or pregnant patients or patients with disorders of the gastrointestinal, gynecologic and genitourinary systems.[15]

Most of the bleeding episodes occur during the first two months or after three years of therapy. Therefore, the patient should be examined weekly in the clinic or office during the first few weeks for (1) detection of bleeding, (2) stabilization of drug dosage by monitoring the one-stage prothrombin times and (3) review of the patient's understanding and management of his or her own treatment. Physicians who are experienced in administering anticoagulant therapy provide their patients with detailed verbal and written instructions that (1) explain the danger signs of bleeding and symptoms of recurrent thromboembolic disease, (2) note the times to contact the physician, (3) warn the patient about relying on memory for the size and frequency of the drug dose, (4) urge the use of a calendar or diary for recording the amount of drug actually taken and (5) remind the patient to either carry on his or her person a wallet card or to wear a Medic-Alert bracelet or "dog-tag" necklace to alert medical

personnel in an emergency. Experienced physicians also give a supply of vitamin K_1 tablets to their patients for emergency use. Yet despite this detailed care, *bleeding often occurs even when the prothrombin time is within the expected therapeutic range,*[12] as happened in Dr. Honoré's patient. It is this aspect above all—the near-fatal bleeding when the patient's prothrombin time was only twice the control value—that gives such heuristic value to the case report in this issue.

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